



# Knowledge Based Oncology: Ontologia e Large Databases



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# *Knowledge Based Oncology*

## INDIVIDUALIZED

Tailoring treatments by  
prognostic/predictive  
features

**Clinical  
decision**

## MODELLING

Prediction by  
multidimensional (large)  
databases

Propagation of dynamic  
representation of  
knowledge

## ADAPTIVE

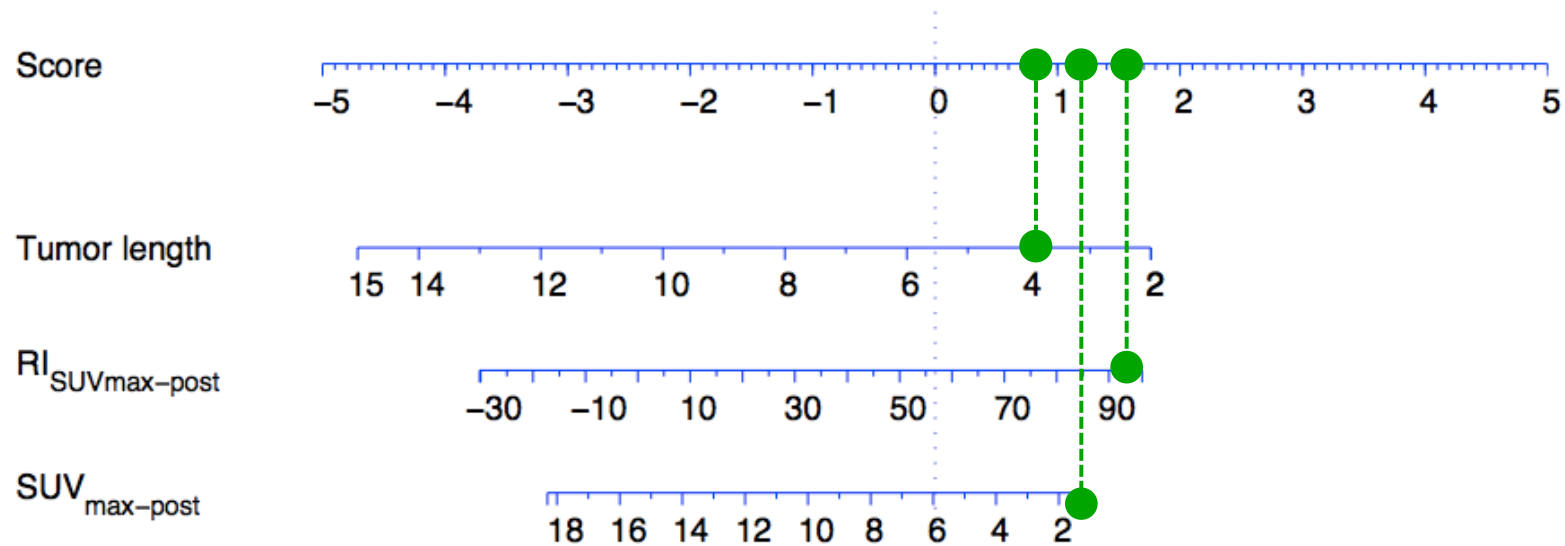
Tailoring treatments  
by continuous  
monitoring





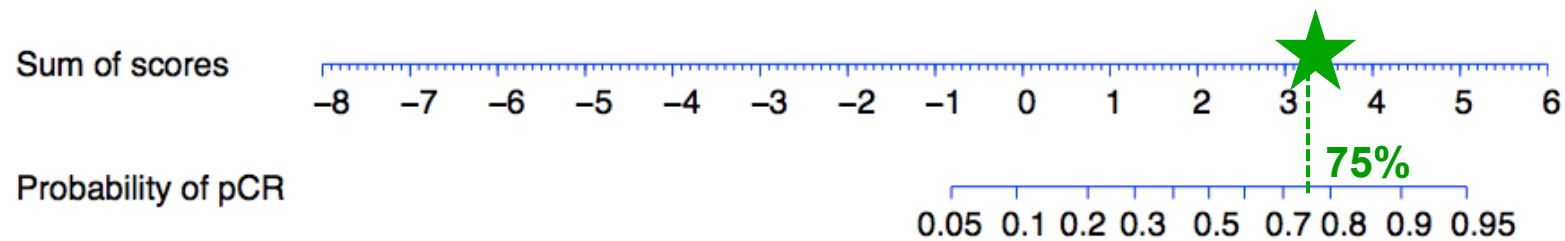
# Nomogram

*pCR*



Sum of scores 3.3

AUC = 0.86





# Nomograms in Breast Cancer



Memorial Sloan-Kettering  
Cancer Center

[Prediction Tools](#) ▶ [Breast Cancer Nomograms](#) ▶ [Sentinel Lymph Nodes Metastasis](#)

mskcc.org  
PREDICTION TOOLS

## Breast Cancer Nomogram: Sentinel Lymph Node Metastasis

TEXT SIZE

This nomogram can be used to help newly diagnosed breast cancer patients assess the likelihood that their breast cancer has spread to the [sentinel lymph nodes](#).

### Enter Your Information

[Clear](#) [Calculate](#) ▶

#### Current Age

Enter current age. Must be between 20 and 91.

years old (20 to 91)

#### Breast Tumor Size

Size of the primary tumor (as measured either in imaging study or pathological exam), in centimeters.

(0.1 cm to 11.0 cm)

#### Special Type?

Check box if tumor has been pathologically defined as pure tubular, pure colloid (mucinous), or typical medullary carcinomas on the pathology report. Other histologies such as atypical medullary carcinoma or carcinoma with ductal and lobular features should be classified as ductal – see Tumor Type and Grade section below for more details.

☐ YES

#### Tumor is confined to UIQ?

Check box if tumor is confined within the upper inner quadrant (UIQ) of the breast.

☐ YES

### Your Results

[Learn more](#) about your results below.

[Probability of Spread to  
Sentinel Lymph Nodes](#)

[Print These Results](#)

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## Breast Cancer Nomogram to Predict Additional Positive Non-SLN, without Neoadjuvant Chemotherapy

This software calculates the probability of finding additional positive non-sentinel lymph nodes in breast cancer patients found to have disease on sentinel lymph node biopsy without completion of neoadjuvant chemotherapy. This nomogram was developed at the University of Texas M. D. Anderson Cancer Center and has been externally validated.

[Enter SLN metastasis size as a categorical variable \(ITC, micrometastasis or macrometastasis\).](#)

Histology:

Choose the histologic type of the tumor. The "Other" category includes mucinous, tubular, papillary and medullary tumors.

Select

Tumor Size:

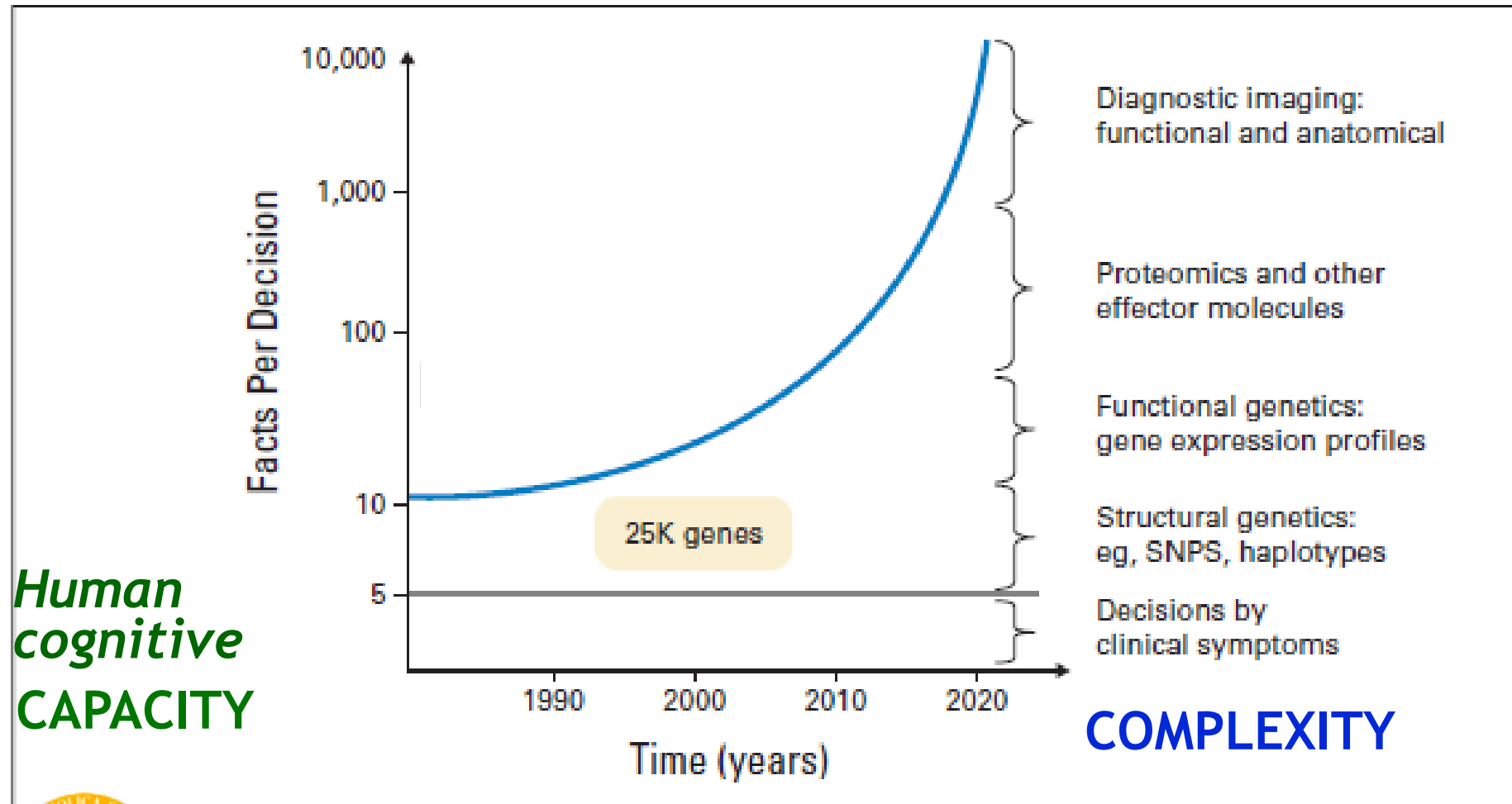
Size of the primary tumor, in centimeters, on surgical pathology.

(cm)





# Complexity and Prediction



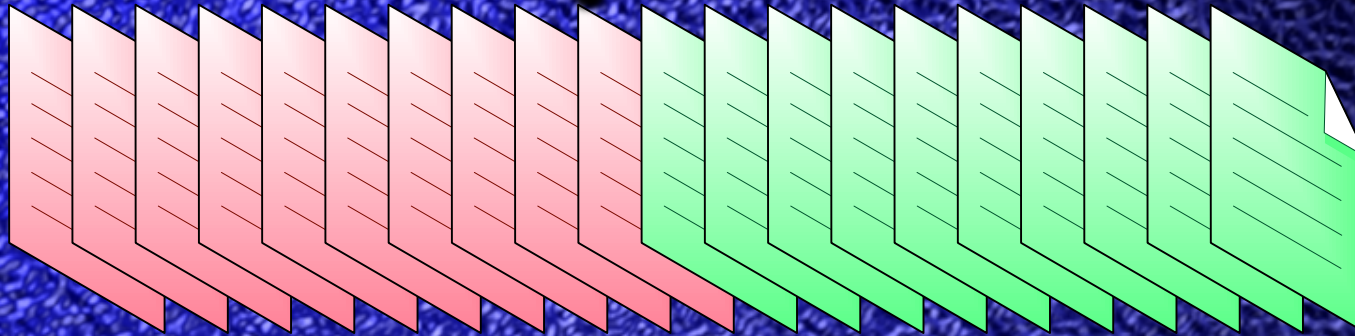
**Abernethy AP et Al – JCO - 2010**



# Complexity and Prediction

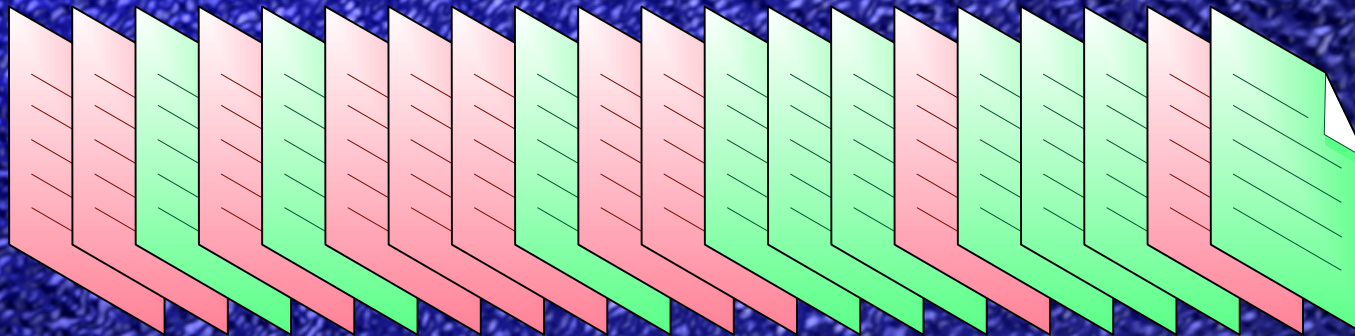
## Experiment

A



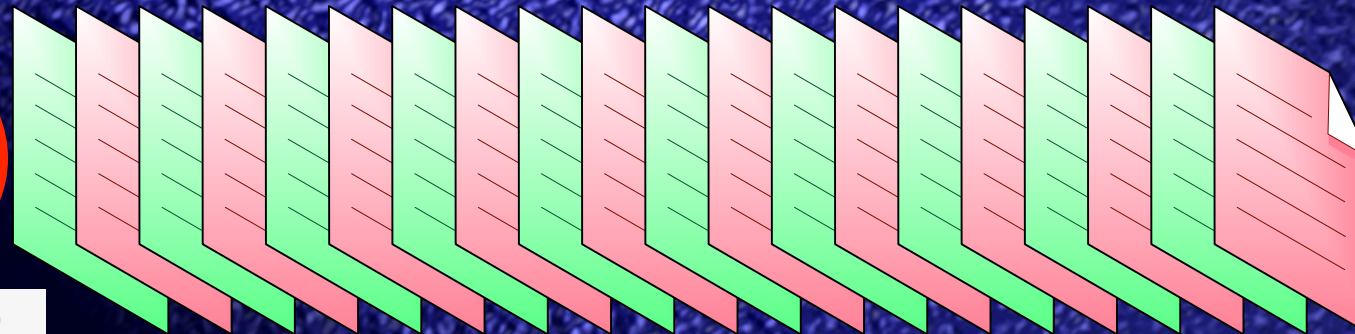
AUC  
1.0

B



AUC  
0.7

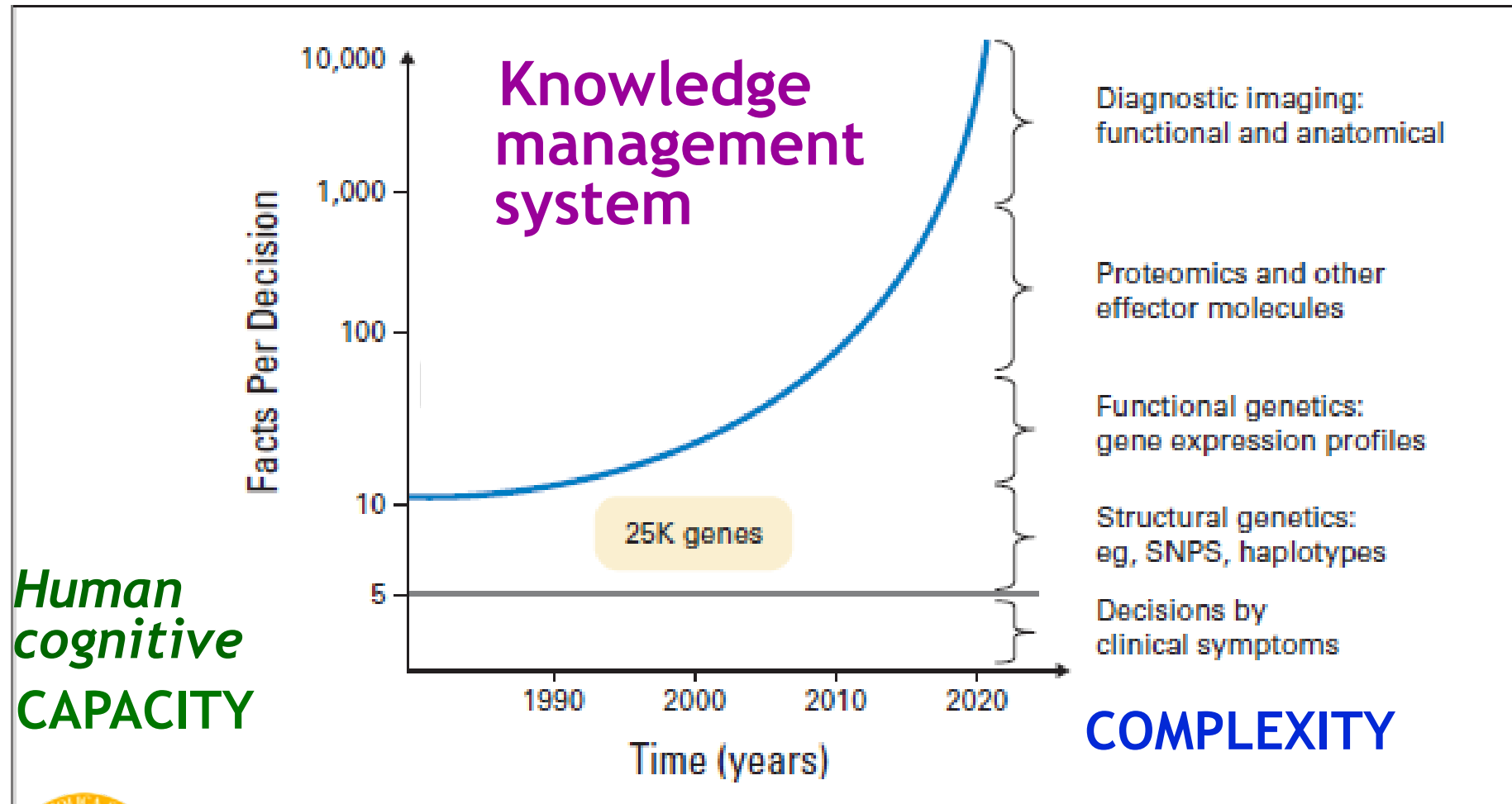
C



AUC  
0.5

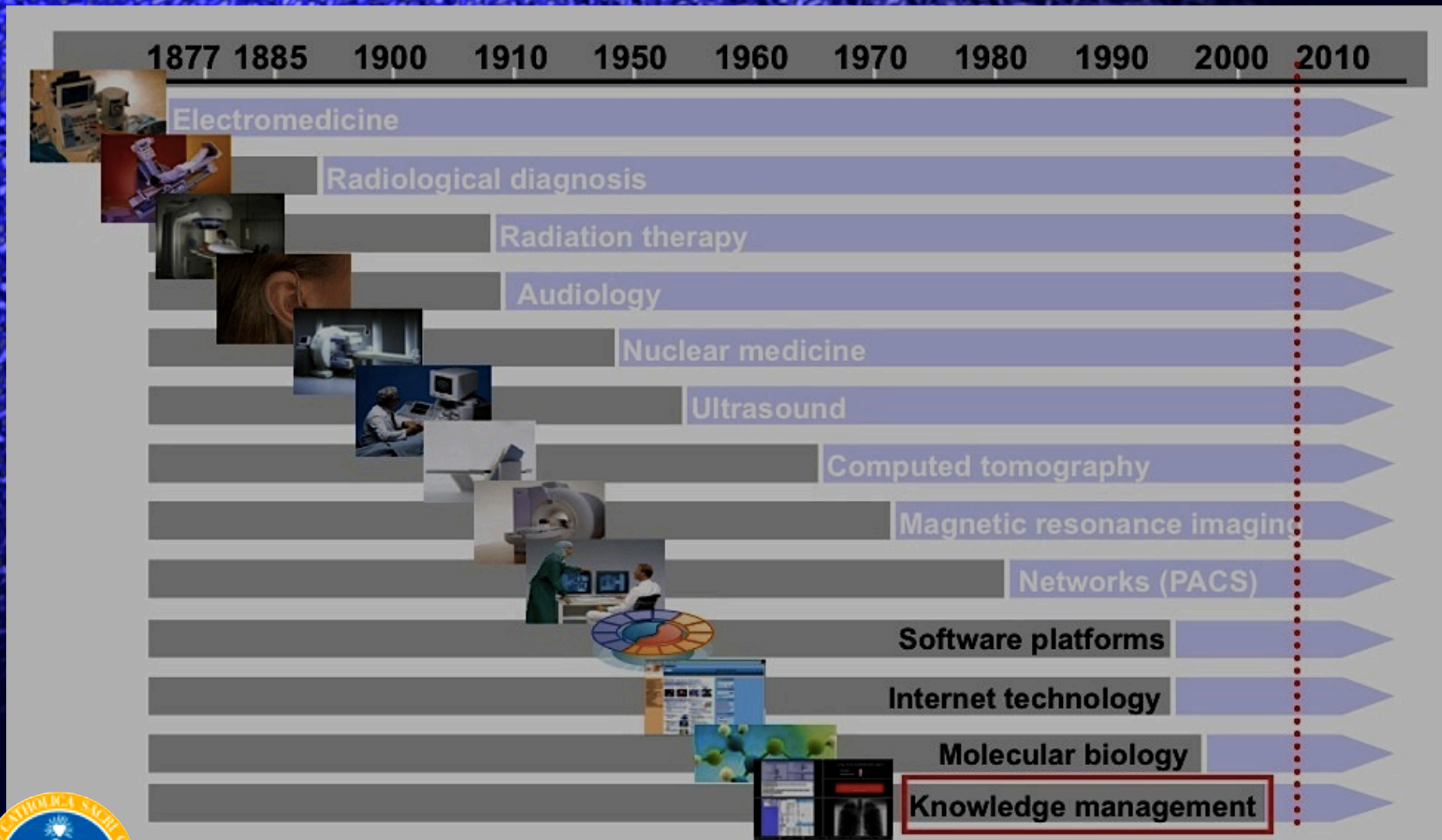


# Complexity and Prediction



**Abernethy AP et Al – JCO - 2010**

# Knowledge Based Technology





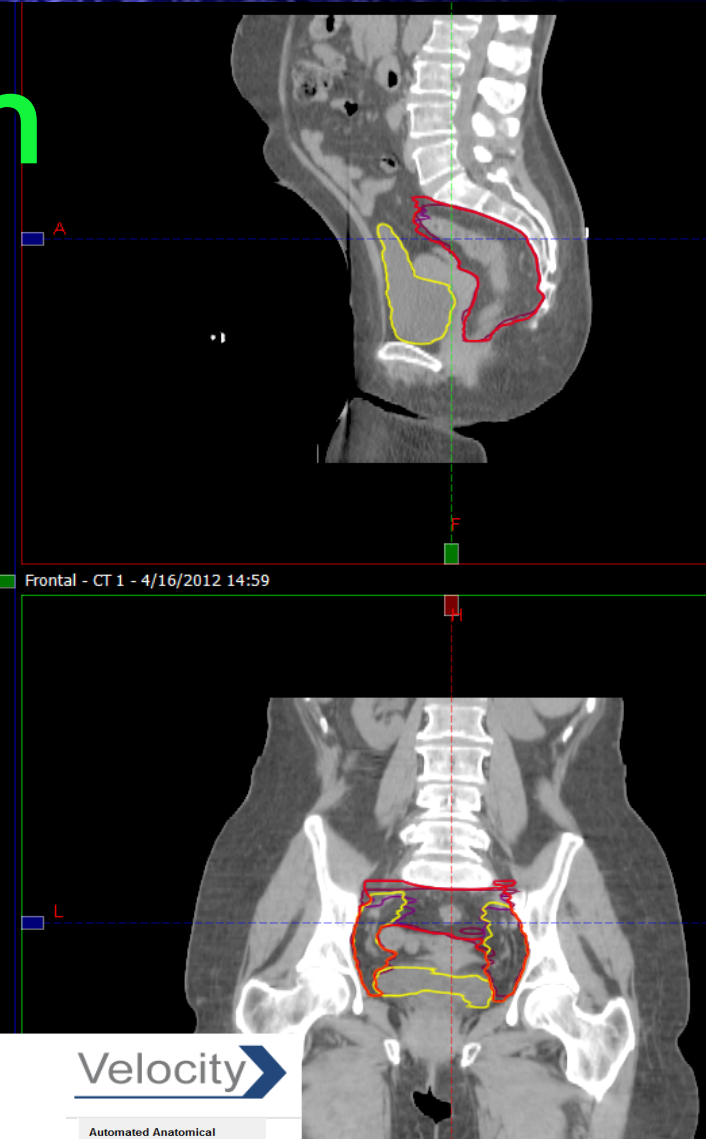
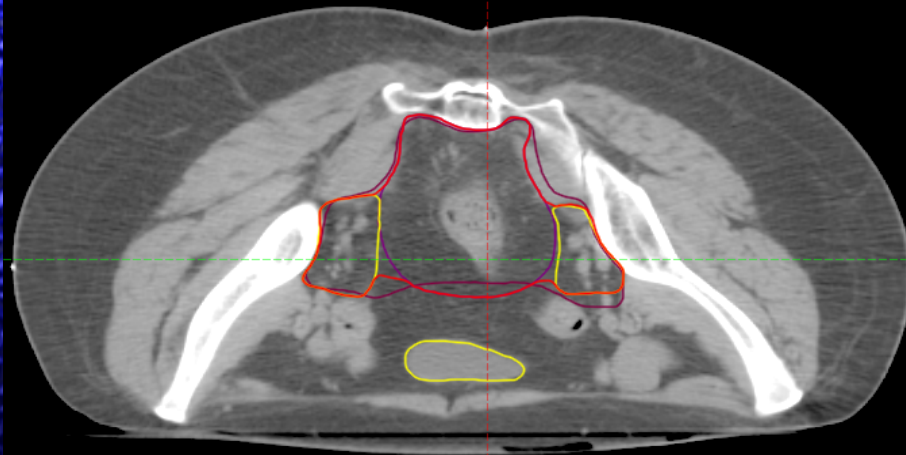
# Knowledge Based Technology





# Knowledge Based Technology

## Autodelineation



Smart Segmentation™



- Automated Anatomical Segmentation
- Deformable atlas-based segmentation
  - Advanced contouring platform
  - Automated PET contouring



# Knowledge Based Contouring

Ontology

Benchmark

Evaluation methods





# ONTOLOGIA

Definizione: deriva dal greco

**ὄντος (òntos)** = pp del verbo εἶμι (eimi) – essere

**λόγος (lògos)** = discorso, studio, scienza

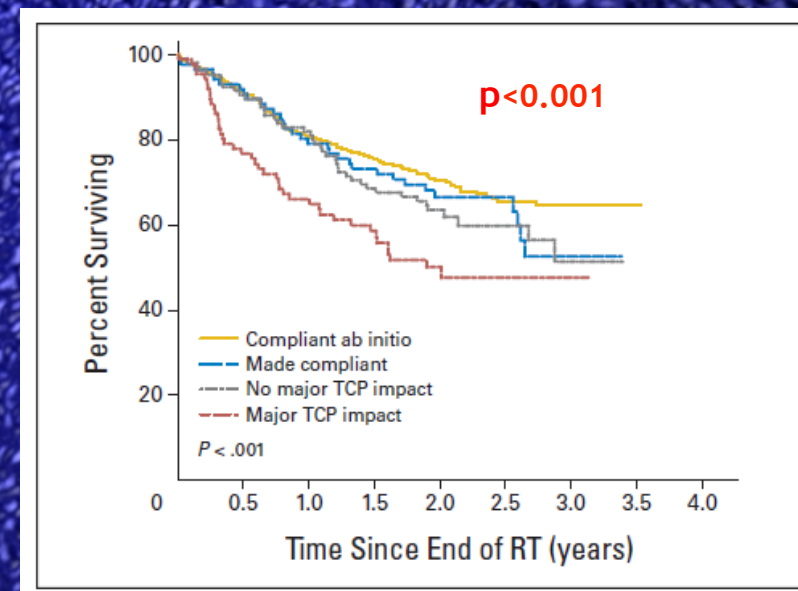
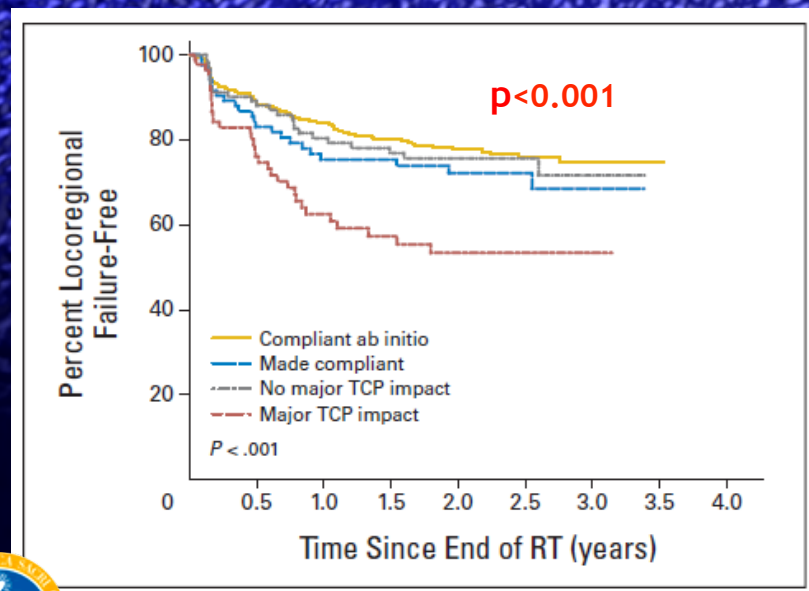
Formalmente intesa come **conoscenza** di un **insieme di variabili** riguardanti un argomento, rappresenta una sorta di **dizionario** che **standardizza terminologie mediche e tecniche di trattamento**.





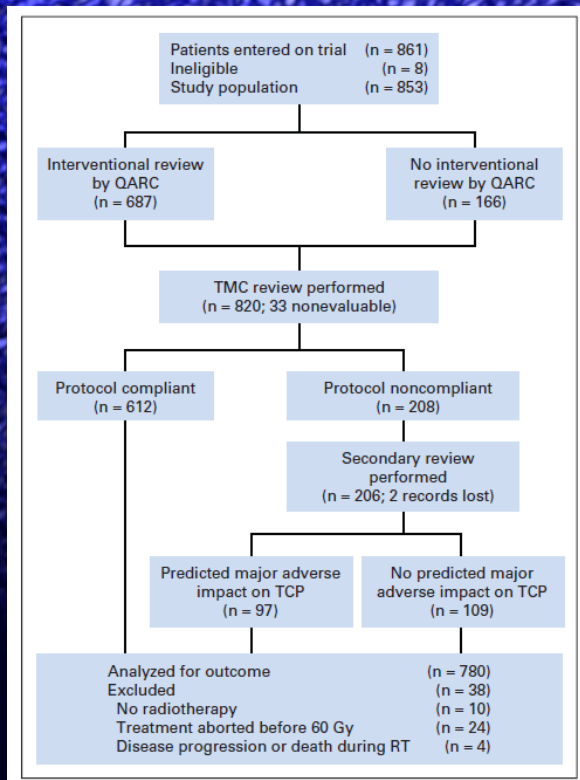
## Critical Impact of Radiotherapy Protocol Compliance and Quality in the Treatment of Advanced Head and Neck Cancer: Results From TROG 02.02

Lester J. Peters, Brian O'Sullivan, Jordi Giralt, Thomas J. Fitzgerald, Andy Trotti, Jacques Bernier, Jean Bourhis, Kally Yuen, Richard Fisher, and Danny Rischin



# Critical Impact of Radiotherapy Protocol Compliance and Quality in the Treatment of Advanced Head and Neck Cancer: Results From TROG 02.02

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**Table 1.** Protocol-Specified Criteria for Significant Deviations

## Tumor

Dose at 2 Gy/fraction delivered to target volumes\*

All gross disease (except nodes < 2 cm) must receive at least 66.5 Gy

No more than 10% of the planning target volume (PTV) enclosing gross disease must receive < 66.5 Gy (< 57 Gy for small nodes) or > 75 Gy, excluding volumes within the gross tumor volume or air cavities

No more than 10% of PTV defining electively treated areas must receive < 40 Gy

## Treatment prolongation

Overall treatment time must not exceed 9 weeks

## Normal tissues

Maximum dose to spinal cord must not exceed 50 Gy

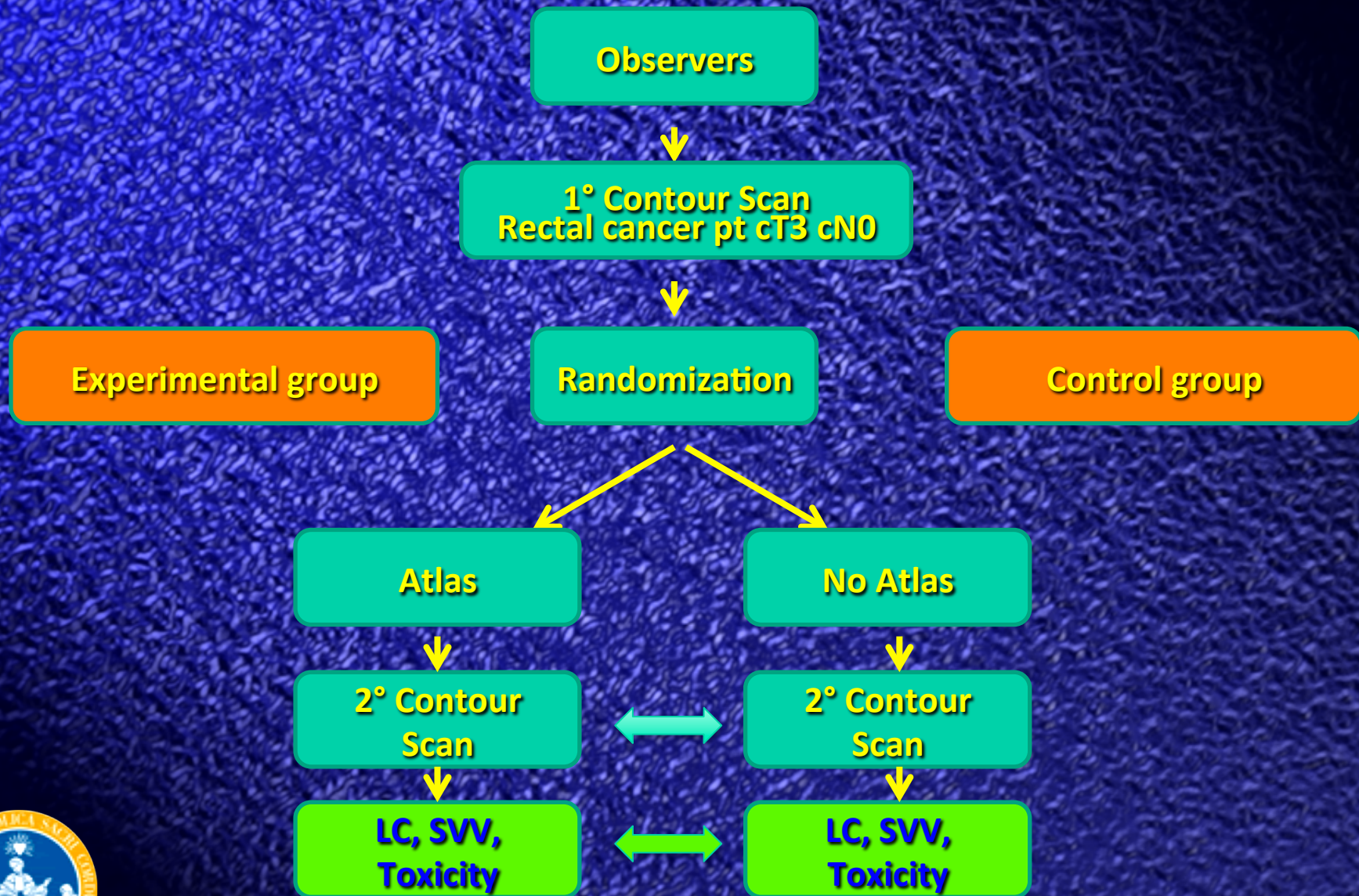
Volumes and doses to uninvolved normal tissues must not be excessive

\*If volumes are incorrectly drawn, deviation assessments will be made on corrected volumes.





# To test delineation reliability

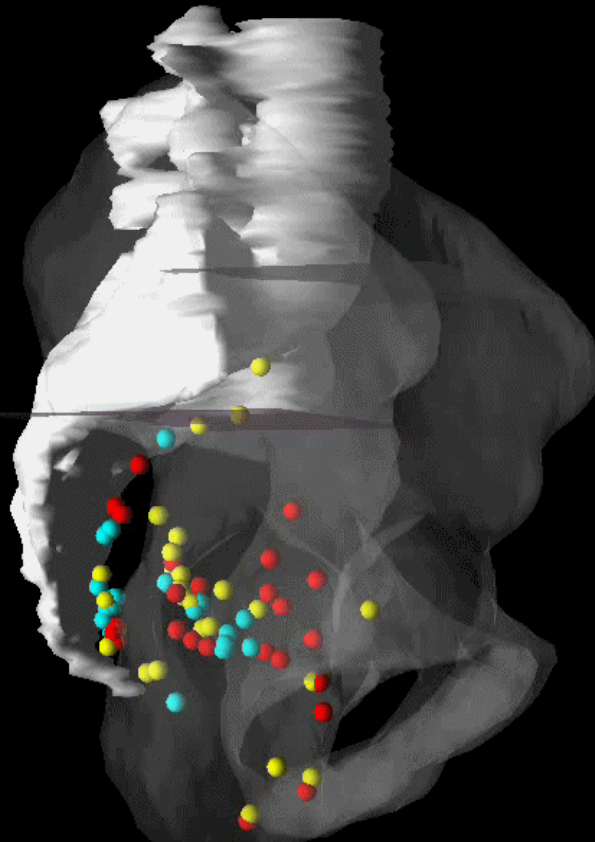


Fuller et al – IJROBP - 2001



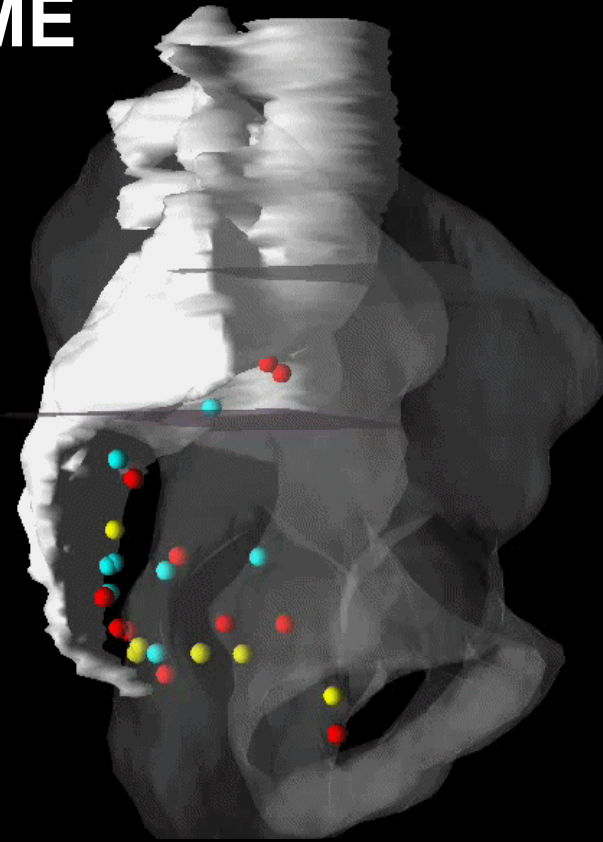
# Area at risk for local recurrence

TME



N0: n = 18  
N1: n = 27  
N2: n = 24

RT + TME



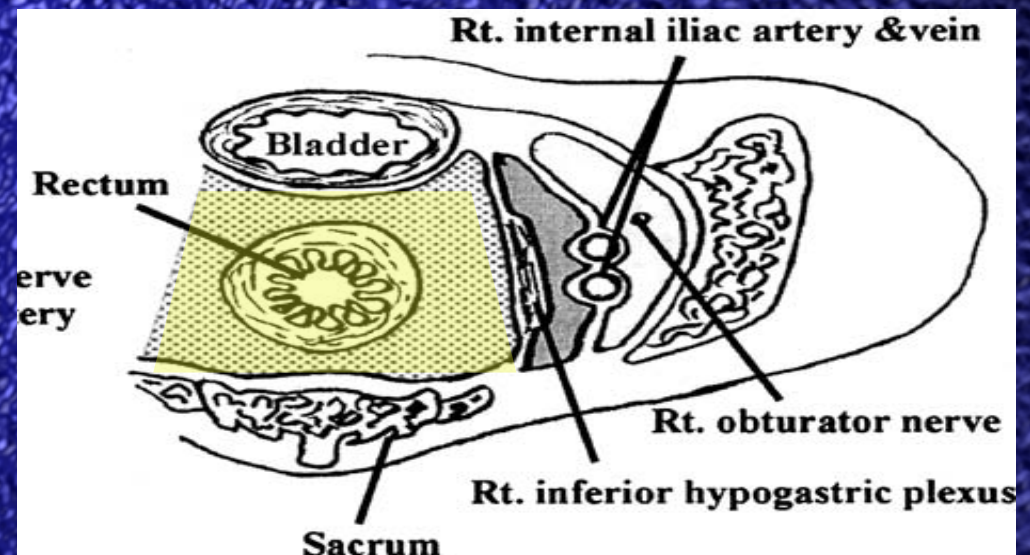
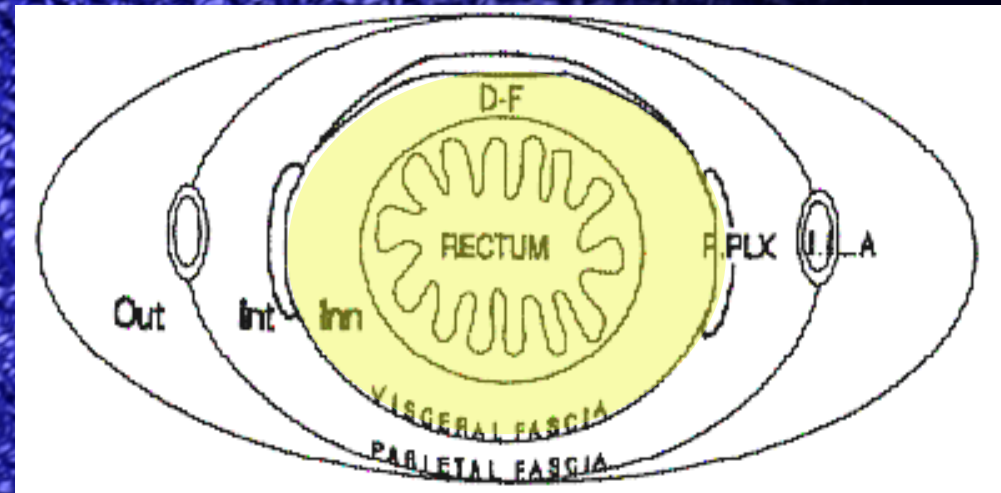
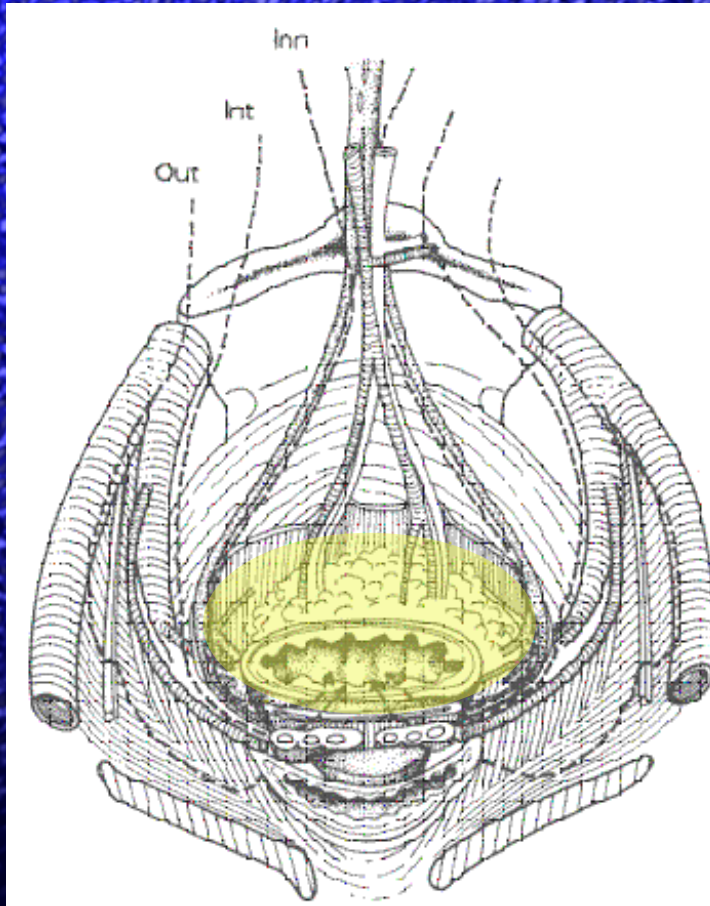
N0: n = 8  
N1: n = 6  
N2: n = 11



Nijkamp J et al – IJROBP – 2011, By the courtesy of C.Marijnen



# ***Pelvic subsites: Japanese perspective***



**Takahashi T et Al – Dis Colon Rectum – 2000**  
**Sato H et Al – Dis Colon Rectum - 2006**

## Frequency of Lateral Lymph Node involvement

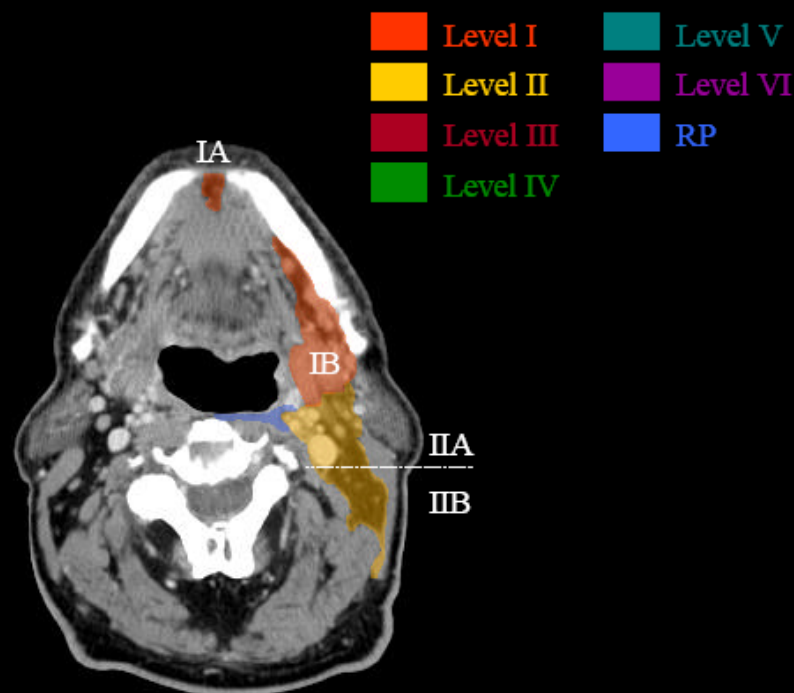
		% positive
pT3		17 %
pT4		23 %
peri-rectal nodes	Negative	6.8 %
	Positive	27.7 %
	pN0	6.8 %
	pN1	24.4 %
	pN2	34.1 %

Ueno et al 2005.





# Atlas Based Delineation: Ontology



WW: 457 WL: -1

V. Gregoire et al. / Radiotherapy and Oncology 80 (2006) 227–236

229

The boundaries of the surgical levels could then be precisely projected onto the matched CT slices.

Although developed with similar objectives, the Iltis and the original Rotterdam guidelines differed substantially. For example, differences existed in the definitions of the cranial border of level II, the posterior border of levels II, III, IV and V, the cranial border of level V and the caudal border of level VI. Readers are referred to the original publications for a comprehensive description of the original recommendations [9,14].

The second simplified version of the Rotterdam guideline was developed not only to substitute boundaries which were easier to identify (e.g. vertebral bodies, salivary glands, pharyngo-laryngeal lumen) than the original anatomical boundaries, but also to allow delineation of different nodal levels on a limited number of CT slices, from which the all neck levels could be reconstructed by interpolation. This simplified protocol substantially reduced the contouring time and allowed selective neck irradiation with similar partial gland sparing compared to the original Rotterdam guidelines. However, differences between the simplified version of the Rotterdam guidelines and the Iltis guideline were even greater than between the original Rotterdam and Iltis guidelines (Fig. 1).

### 3. General methodology used to reach the consensus guidelines for the delineation of the neck node levels

In view of the differences observed between the Iltis and the Rotterdam guidelines, a multidisciplinary working group, including members from both the original Iltis and Rotterdam groups, was created to try to create a unified set of recommendations for the delineation of the various levels in the clinically uninvolved, 'node-negative' neck. Subsequently, the working group was enlarged to include representatives of American and European cooperative groups. All of the physicians who contributed to the creation of these guidelines are listed as co-authors of this manuscript. The general principles which guided the activities of the working group were (1) to translate as accurately as possible the surgical guidelines into radiologic guidelines based on axial CT sections, and (2) to minimize differences in interpretation of the guidelines, by defining less ambiguous boundaries than previously described.

Several factors motivated the panel to use the previously described surgical guidelines as their basic frame of reference. First, perhaps more than anywhere else, achievements in head and neck oncology have resulted from complementary interactions of surgery and radiotherapy. This complementarity will become even more critical for future advances based on 3D-CRT and/or IMRT since increasingly more precise target volumes will be delivered to increasingly more precise target volumes. This prompts us to advocate for the use of a similar language to that already used by surgeons for more than a decade. Second, in properly

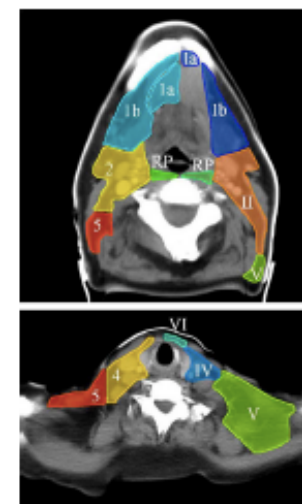


Fig. 1. Comparison between the simplified Rotterdam guideline (left side of the neck, Arrows figure) and the Iltis guideline (right side of the neck, Arrows figure) for the delineation of the neck node levels. On the top, CT slice at the level of the hyoid bone of the mandible, with 1a, 1b, 2 and 3, and retropharyngeal nodes (RP) are displayed. On the bottom, CT slice at the level of the carotid sheath, levels IV, V and VI are displayed.

selected patients, neck node dissection performed according to standardized procedures, removing only selected nodal levels, has produced high rates of control in the pathologically assessed node-negative neck, without post-operative radiotherapy [1]. This observation confirmed that the locations of the lymphatic areas at risk for microscopic infiltration often are well-defined, and retrospectively validated the use of selective tissue dissection as an effective prophylactic treatment modality for the neck of selected patients. Third, to some extent in the past, the selection and the delineation of the target volume for head and neck radiotherapy were driven more by technical limitations than by patient anatomy. This led to unavoidable, unnecessary irradiation of normal tissue bearing little or no risk of tumor cell infiltration, with the potential risk of acute and/or late complications of treatment. In this framework, the use of



Gregoire V et al – Radioth & Oncol – 2006



# Atlas Based Delineation: Semantic

H&N

**Results:** Inclusion of the retrostyloid space cranially and the supra-clavicular fossa caudally is proposed in case of neck nodes (defined radiologically or on the surgical specimen) located in levels II, and IV or Vb, respectively. When extra-capsular rupture is suspected (on imaging) or demonstrated on the pathological specimen, adjacent muscles should also be included in the CTV. For node(s) located at the boundary between contiguous levels (e.g. levels II and Ib), these two levels should be delineated. In the post-operative setting, the entire 'surgical bed' should be included. Last, the retropharyngeal space should be delineated in case of positive neck from pharyngeal tumors.

Rectum

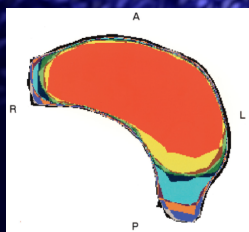
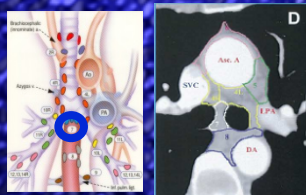
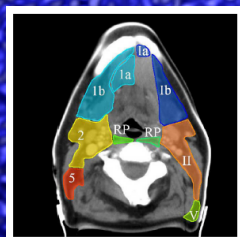
	Cranial	Caudal	Anterior	Posterior	Medial	Lateral	
Mesorectum	Bifurcation of the inferior mesenteric artery (IMA) in sigmoid and superior rectal artery	Insertion of the levator ani muscle into the rectal wall/disappearing of mesorectal fat tissue around the rectum	<i>Superior:</i> Anterior limit of superior rectal vessels or a virtual line between the anterior aspect of internal iliac vessels of both sides <i>Inferior:</i> Bladder, prostate/seminal vesicle in man, vaginal wall/uterus in woman	<i>Superior:</i> Mesorectal fascia in front of sacral concavity <i>Inferior:</i> Levator ani muscle		<i>Superior:</i> Mesorectal fascia/internal and external iliac lymph node area <i>Inferior:</i> Levator ani muscle	tal
cT3 high the peritoneal reflection							
cT3 mid-l (at the peritoneal reflection)	Presacral space (posterior pelvic subsite)	Sacral promontory	Coccyx	<i>Superior:</i> 1 cm in front of the bone <i>Mid-inferior:</i> Presacral fascia/posterior mesorectal fascia	Sacral concavity	Lateral border of the sacrum	irect
Any cT with massive pelvic lymph node regions	Internal iliac nodes (lymph node regions)	Bifurcation of common iliac artery into internal and external iliac arteries (bony reference L5-S1)	Ending of the mesorectum/appearance of ischio-rectal fossae	<i>Superior:</i> Behind the external iliac vessels <i>Mid-inferior:</i> Behind obturator nerve	Lateral edge of the sacro-iliac joint Pyriform muscle	Mesorectal fascia, pelvic organs <i>Superior:</i> Psoas muscle and ileum <i>Inferior:</i> Internal obturator muscle	irect
Any cT with massive pelvic lymph node regions	Obturator nodes (lymph node regions)	Caudal border of sacro-iliac joint	The entrance of the obturator nerve/artery in the obturator canal	Posterior aspect of the external iliac vessels	Posterior aspect of the obturator nerve	Mesorectal fascia, pelvic organs Internal obturator muscle and ileum	irect
Any cT with massive pelvic lymph node regions	External iliac nodes (lymph node regions)	Bifurcation of common iliac artery into internal and external iliac arteries (bony reference L5-S1)	The start of the femoral vessels	<i>Superior-mid:</i> 0.7 cm from the vessel <i>Inferior:</i> Abdominal wall muscles	Posterior aspect of the external iliac vein	Mesorectal fascia, pelvic organs Psoas muscle, iliac muscle	irect
cT4 with anterior pelvic organ	Sphincter complex Inferior pelvic subsite (ischio-rectal fossae)	1.5 cm around the internal and external anal sphincters Levator ani muscle	Skin	Obturator muscle	A virtual line between the posterior profile of the gluteus muscle of both sides	Anal canal Obturator muscle and gluteus muscle	irect



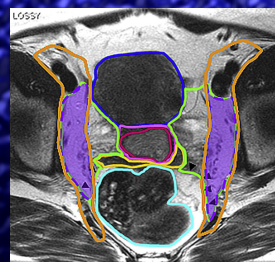
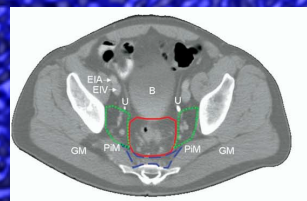
Gregoire V et al – Radioth & Oncol – 2006  
Gambacorta MA et al – M. M. Rectal Cancer -2012



# Atlas Based Delineation: Ontology



Site	Author	Number	Endorsment
H&N	Martinez-Monge R, 1999 Gregoire et al, 2000, 2003, 2006 <sup>1</sup> Vorwerk H, 2011	3	DAHANCA <sup>1</sup> , EORTC <sup>1</sup> , GORTEC <sup>1</sup> , NCIC <sup>1</sup> , RTOG <sup>1</sup>
Lung	Martinez-Monge R, 1999 Chapet, 2005 Kong FM, 2011 <sup>1</sup>	3	EORTC <sup>1</sup> , RTOG <sup>1</sup> , SWOG <sup>1</sup>
Breast	Martinez-Monge R, 1999 Madu CN, 2001 Dijkema IM, 2004 Kirova YM, 2009 RTOG Breast Cancer Contouring Atlas ( <a href="http://www.rtog.org">http://www.rtog.org</a> ). Belaid A, 2010 Atean <sup>1</sup> , 2012	7	RTOG  SFRO <sup>1</sup>



Site	Author	Number	Endorsment
Stomach	Martinez-Monge R, 1999 Cellini F, 2003 Matzinger O, 2009 <sup>1</sup>	3	EORTC-ROG <sup>1</sup>
Pancreas	Martinez-Monge R, 1999 Sun W, 2010 Caravatta, 2012 Goodman KA, 2012 <sup>1</sup>	4	RTOG <sup>1</sup>
Ano-Rectum	Martinez-Monge R, 1999 Arcangeli S, 2003 Roels S, 2006 Myerson RJ, 2009 <sup>1</sup> Ng M, 2011 <sup>2</sup> Gay HA, 2012 (OaRs) <sup>1</sup> Gambacorta M.A., 2012	7	RTOG <sup>1</sup> AGITG <sup>2</sup>
Gyn	Martinez-Monge R, 1999 Taylor A, 2005 Portaluri M, 2005 Taylor A, 2007 Small W, 2008 <sup>1,3-6</sup> Toita T, 2010 <sup>2</sup> Lim 2011 <sup>1</sup> Gay HA, 2012 (OaRs) <sup>1</sup>	8	RTOG <sup>1</sup> GCSG <sup>2</sup> GOG <sup>3</sup> NCIC <sup>4</sup> ESTRO <sup>5</sup> ACRIN <sup>6</sup>
Prostate	Martinez-Monge R, 1999 Poortmans P, 2007 <sup>2</sup> Wiltshire KL, 2007 Sidhom MA, 2008 <sup>3</sup> Lawton CAF, 2009 Michalski JM, 2010 <sup>1</sup> Gay HA, 2012 (OaRs) <sup>1</sup>	7	RTOG <sup>1</sup> EORTC <sup>2</sup> FROGG <sup>3</sup> RANZRC <sup>3</sup>



Atlas Based Delineation: Ontology

# Atlas Based Propagation Troubles

- One Master
- Many Masters
- Many Atlases





# Knowledge Based Contouring

Ontology

Benchmark

Evaluation methods



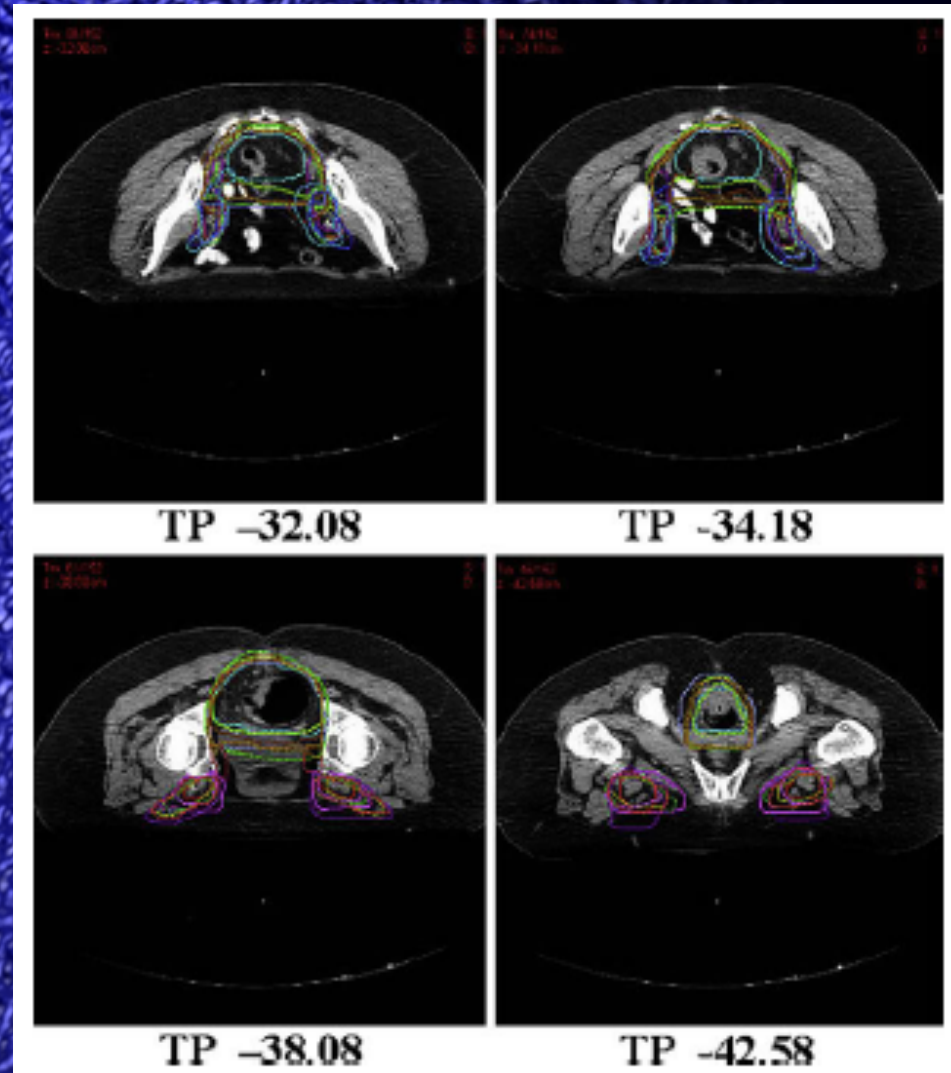


# Atlas Based Delineation: Benchmark

Table 1. Preconsensus statistical analysis of agreement level

CTV	STAPLE estimates		$\kappa$ Statistics agreement
	Sensitivity	Specificity	
CTVA	$0.83 \pm 0.18$	$0.96 \pm 0.04$	$0.68 (p < 0.0001)$ "Substantial"
CTVB	$0.61 \pm 0.18$	$0.99 \pm 0.02$	$0.49 (p < 0.0001)$ "Moderate"
CTVC	$0.66 \pm 0.21$	$0.98 \pm 0.04$	$0.49 (p < 0.0001)$ "Moderate"

Abbreviations: CTV = clinical target volume; STAPLE = simultaneous truth and performance level estimation.



Myerson R et al – IJRBOP – 2008





# Atlas Based Delineation: Benchmark

study to RTOG 0529, incorporating cetuximab with standard 5FU and mitomycin-C for anal canal cancer. In these studies, particular attention will be warranted to the patterns of recurrence, to ensure that these CTV consensus panel recommendations, as well as the use of IMRT for the management of anorectal cancers, are appropriate.

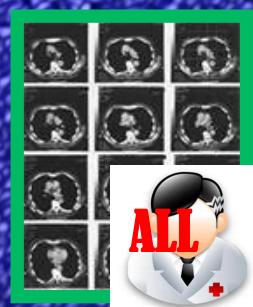




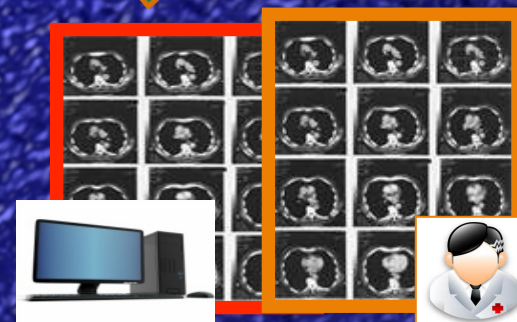
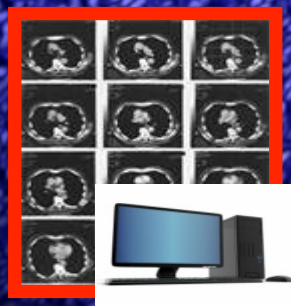
# Atlas Based Delineation: Benchmark



Similarity Value  
0.78



Similarity Value  
0.84



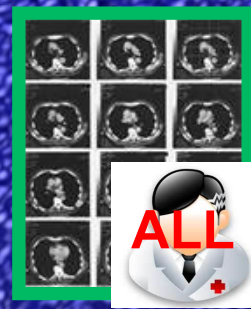


# Ready Rectal 02



Similarity Value  
**0.84**

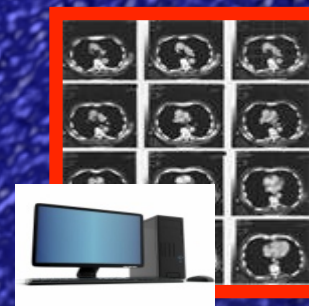
Similarity Value  
**0.75**



**Master  
(30 pts)**



**Manual (15 + 15 pts)**



**Automatic (30 pts)**





# Knowledge Based Contouring

Ontology

Benchmark

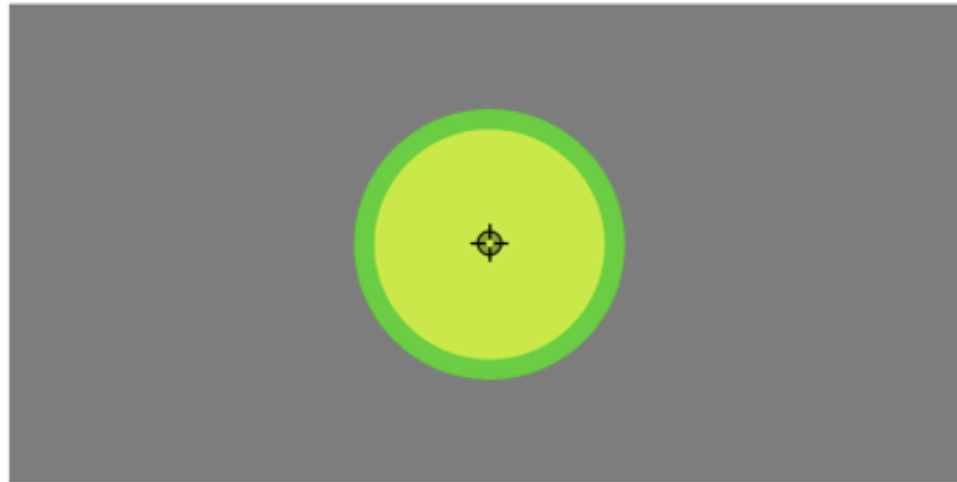
Evaluation methods





# Atlas Based Delineation: Evaluation

*Dice, Jaccard and CN indexes: a comparison*

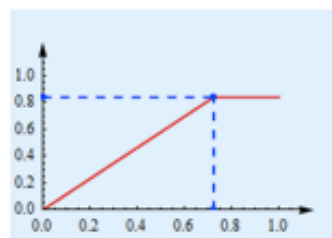


**0.72**

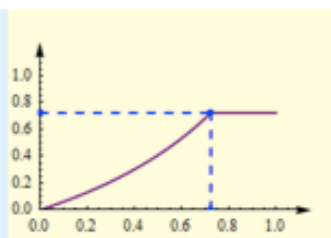
Green Area:	1.0000
Yellow Area:	0.7240
Intersection Area:	0.7240
Dice Index	0.8400
Jaccard Index	0.7240
Conformation Number	0.7240
Hausdorff Distance	0.0842

**0.84**  
**0.72**  
**0.72**

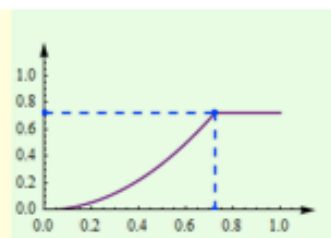
*DICE Index*



*Jaccard Index*



*Conformation Number*



*A. Damiani and V. Valentini UCSC Rome – July 2013*

Yellow Area ☐

Make areas equal ☐

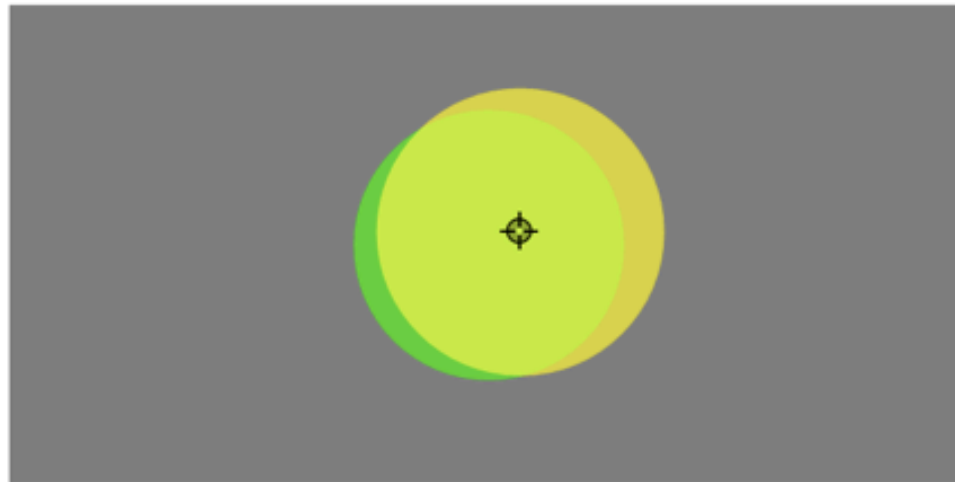
Make concentric ☐





# Atlas Based Delineation: Evaluation

*Dice, Jaccard and CN indexes: a comparison*

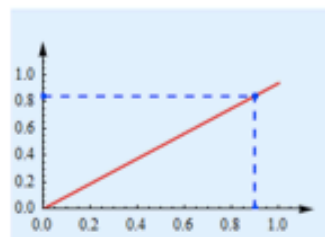


**0.89**

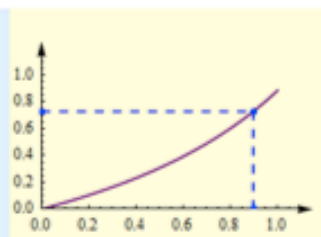
Green Area:	1.0000
Yellow Area:	1.1300
Intersection Area:	0.8970
Dice Index	0.8420
Jaccard Index	0.7280
Conformation Number	0.7120
Hausdorff Distance	0.1760

**0.84**  
**0.72**  
**0.72**

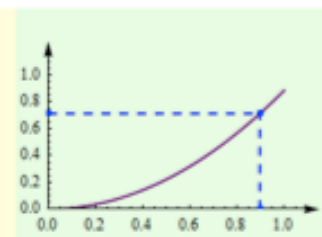
*DICE Index*



*Jaccard Index*



*Conformation Number*



*A. Damiani and V. Valentini UCSC Rome - July 2013*



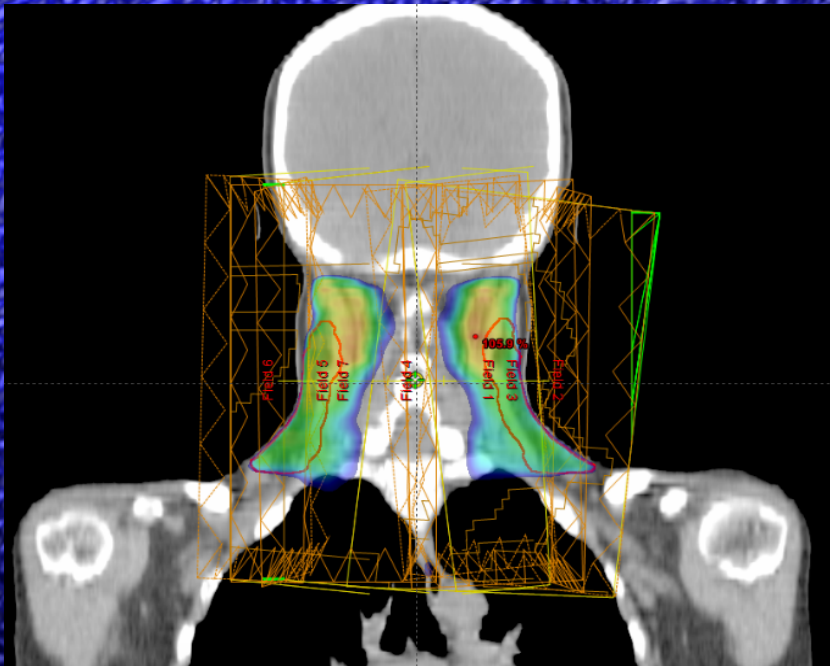
Yellow Area ☐

Make areas equal ☐

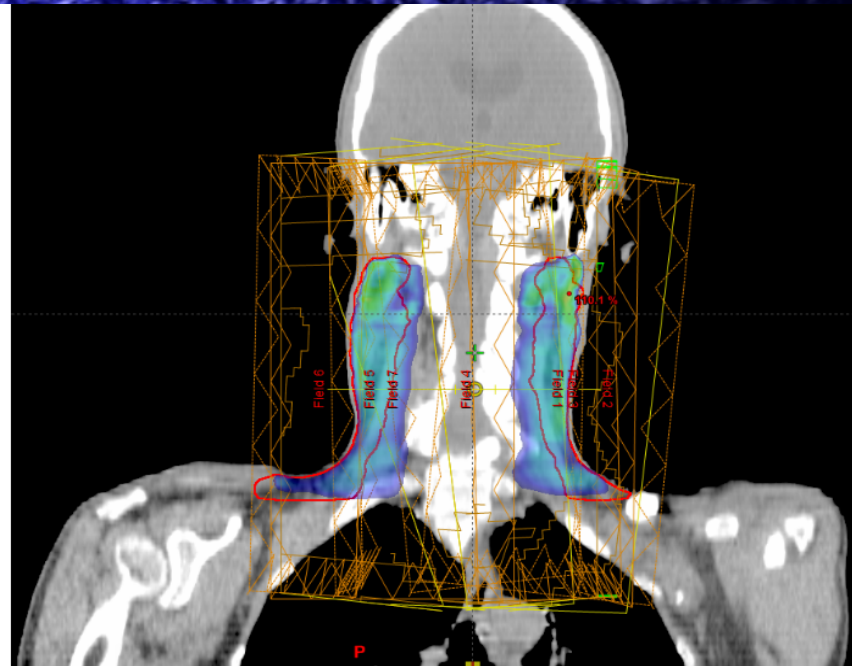
Make concentric ☐



# Atlas Based Delineation: Evaluation



**BvsC DSI 0.91 PTV V95 = 96.1%**



**BvsC DSI 0.9 PTV V95 = 90.8%**






# *Knowledge Based Technology*

## Static vs dynamic Knowledge





# Knowledge Based Technology



## GRAND ROUNDS

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Professor of Rheumatology  
St. Bartholomew's and The London NHS Trust, UK

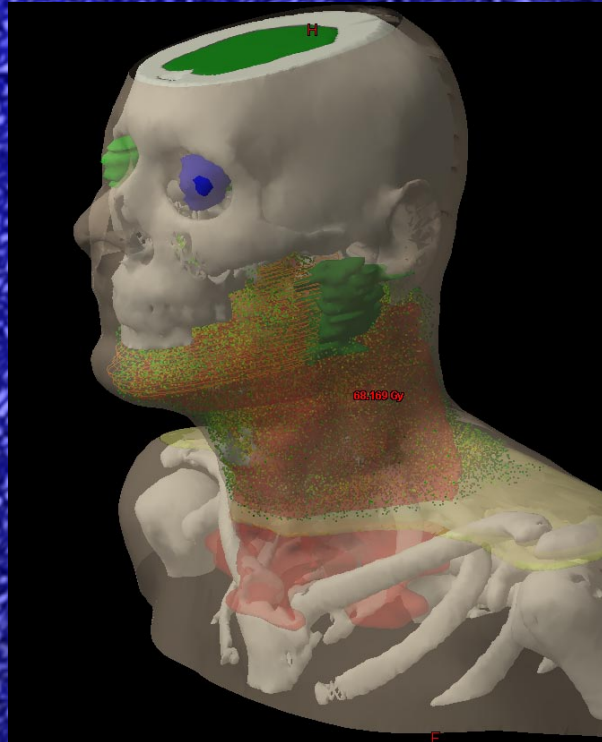
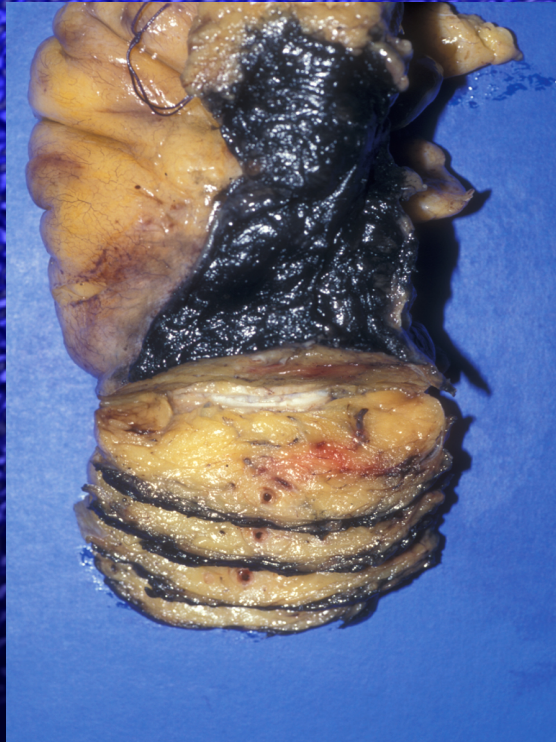
**GRAND ROUNDS:**  
*Case reports with medical educational value*



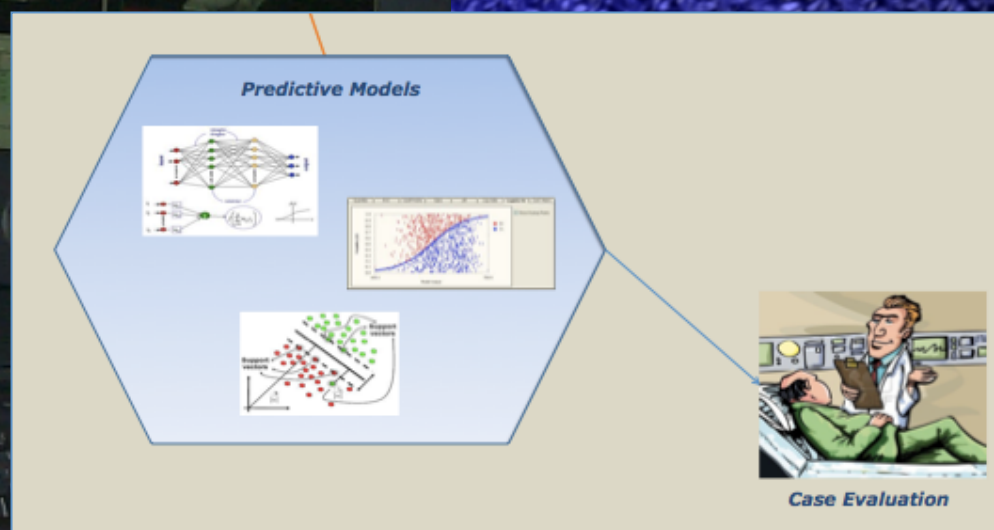
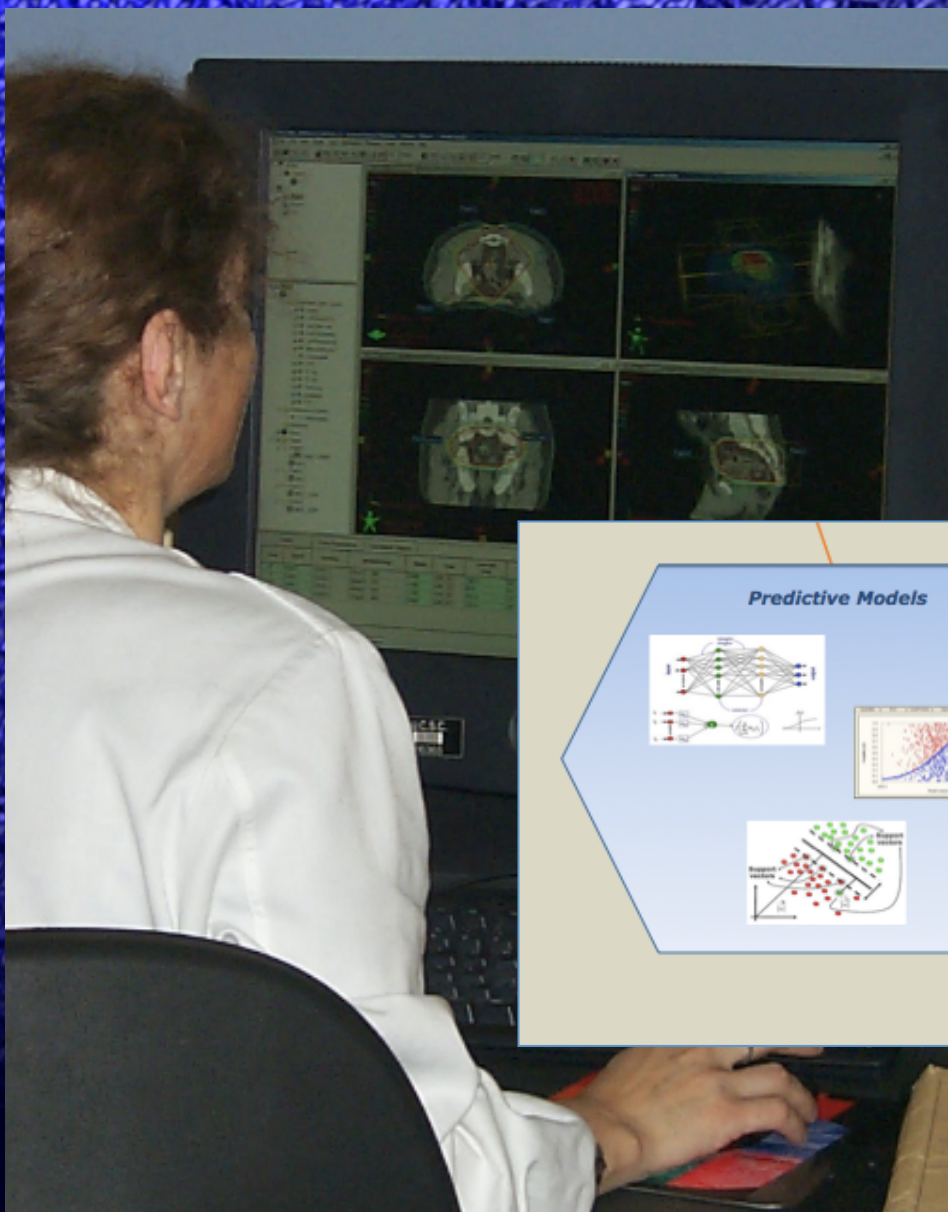


# *Knowledge Based Oncology*

## The Radiation Oncology privilege

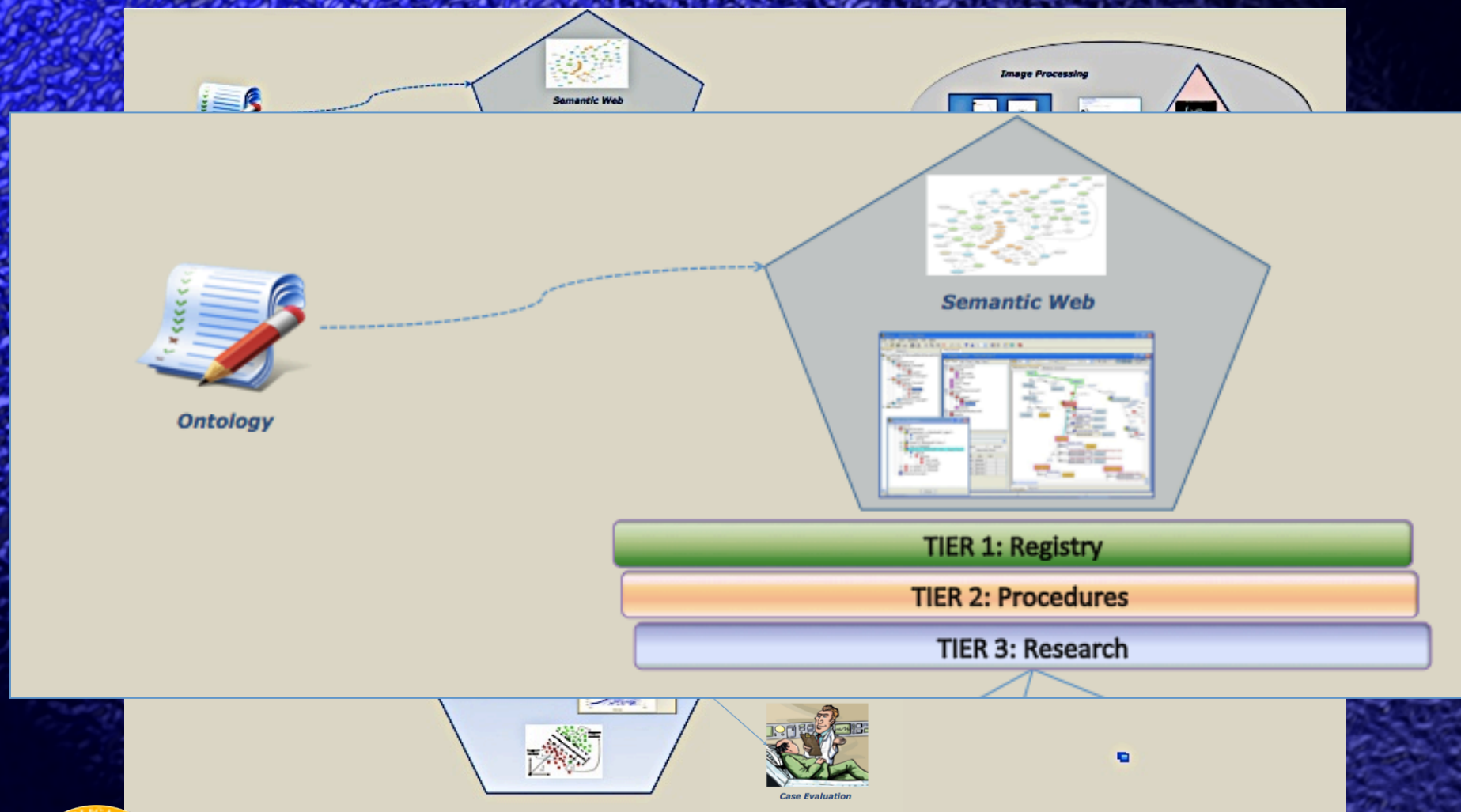








# Project aim





# ONTOLOGIA TUMORE DEL RETTO

- 209 variabili analizzate:
  - Registry level: variabili paziente correlate

(  
a

Registry Level		
Table. 1 Overview data collection – VATE Project		
Variables	Definition	Measurement
<b>Eligibility criteria</b>		
Rectal Cancer	According to the ICD-9 classification	0: 154.0 Rectosigmoid junction 1: 154.1 Rectum 999: missing data
<b>General characteristics</b>		
Institute	Hospital/Institute where patient was treated	Europe: EU-Country code (CC)-Institute number (IN) North America: AN-CC- IN South America: AS-CC-IN Asia: AA-CC-IN Australia: AU-CC-IN
Age@RT	at start of radiotherapy treatment (first fraction)	years
Age@Diagnosis	At diagnosis	years
Gender	Male/female	M: male F: female
Ethnicity		<b>Table 1</b>
<b>Outcome</b>		
Death		0: No – last FUP data 1: Yes – data of death
Cause of death		0: Tumor disease 1: Other





# ONTOLOGIA TUMORE DEL RETTO

- 209 variabili analizzate:
- Procedure level: **presentazione clinica e**

8	Irinotecan
9	Cetuximab (Erbix)
10	Bevacizumab (Avastin)
12	Missing data
13	Panitumumab (Vectibix)
14	UFT
15	S-1

table 12: Toxicities - CTC 3.0

		Grade				
Adverse name	Short name	1	2	3	4	5
<b>Blood System Disorders</b>						
Hemoglobin	Hemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 - 8.0 g/dL <6.2 - 4.9 mmol/L <100 - 80 g/L	<8.0 - 6.5 g/dL <4.9 - 4.0 mmol/L <80 - 65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
Leukocytes (total WBC)	Leukocytes	<LLN - 3000/mm <sup>3</sup> <LLN - 3.0 x 10 <sup>9</sup> /L	<3000 - 2000/mm <sup>3</sup> <3.0 - 2.0 x 10 <sup>9</sup> /L	<2000 - 1000/mm <sup>3</sup> <2.0 - 1.0 x 10 <sup>9</sup> /L	<1000/mm <sup>3</sup> <1.0 x 10 <sup>9</sup> /L	Death
Lymphopenia	Lymphopenia	<LLN - 800/mm <sup>3</sup> <LLN x 0.8 - 10 <sup>9</sup> /L	<800 - 500/mm <sup>3</sup> <0.8 - 0.5 x 10 <sup>9</sup> /L	<500 - 200/mm <sup>3</sup> <0.5 - 0.2 x 10 <sup>9</sup> /L	<200/mm <sup>3</sup> <0.2 x 10 <sup>9</sup> /L	Death
Neutrophils/granulocytes (ANC/AGC)	Neutrophils	<LLN - 1500/mm <sup>3</sup> <LLN - 1.5 x 10 <sup>9</sup> /L	<1500 - 1000/mm <sup>3</sup> <1.5 - 1.0 x 10 <sup>9</sup> /L	<1000 - 500/mm <sup>3</sup> <1.0 - 0.5 x 10 <sup>9</sup> /L	<500/mm <sup>3</sup> <0.5 x 10 <sup>9</sup> /L	Death
Platelets	Platelets	<LLN - 75,000/mm <sup>3</sup> <LLN - 75.0 x 10 <sup>9</sup> /L	<75,000 - 50,000/mm <sup>3</sup> <75.0 - 50.0 x 10 <sup>9</sup> /L	<50,000 - 25,000/mm <sup>3</sup> <50.0 - 25.0 x 10 <sup>9</sup> /L	<25,000/mm <sup>3</sup> <25.0 x 10 <sup>9</sup> /L	Death
Febrile neutropenia (fever of unknown origin without clinically or microbiologically documented infection) (ANC <1.0 x 10 <sup>9</sup> /L, fever ≥38.5°C)	Febrile neutropenia	-	-	Present	Life-threatening consequences (e.g., septic shock, hypotension, acidosis, necrosis)	Death
<b>Gastrointestinal Disorders</b>						
Nausea	Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition; IV fluids indicated <24 hrs	Inadequate oral caloric or fluid intake; IV fluids, tube feedings, or TPN indicated ≥24 hrs	Life-threatening consequences	Death
Vomiting	Vomiting	1 episode in 24 hrs	2 - 5 episodes in 24 hrs; IV fluids indicated <24 hrs	≥6 episodes in 24 hrs; IV fluids, or TPN indicated ≥24 hrs	Life-threatening consequences	Death
Anorexia	Anorexia	Loss of appetite without alteration in eating habits	Oral intake altered without significant weight loss or malnutrition; oral nutritional supplements indicated	Associated with significant weight loss or malnutrition (e.g., inadequate oral caloric and/or fluid intake); IV fluids, tube	Life-threatening consequences	Death

Constipation	Constipation	Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema	Persistent symptoms with regular use of laxatives or enemas indicated	Symptoms interfering with ADL; <del>obstruction</del> with manual evacuation indicated	Life-threatening consequences (e.g., obstruction, toxic megacolon)	Death
Diarrhea	Diarrhea	Increase of <4 stools per day over baseline; mild increase in <del>stomach</del> output compared to baseline	Increase of 4 - 6 stools per day over baseline; IV fluids indicated <24hrs; moderate increase in <del>stomach</del> output compared to baseline; not interfering with ADL	Increase of ≥7 stools per day over baseline; incontinence; IV fluids ≥24 hrs; hospitalization; severe increase in <del>stomach</del> output compared to baseline; interfering with ADL	Life-threatening consequences (e.g., hemodynamic collapse)	Death
Hemorrhoids	Hemorrhoids	Asymptomatic	Symptomatic; banding or medical intervention indicated	Interfering with ADL; interventional radiology, endoscopic, or operative intervention indicated	Life-threatening consequences	Death
Incontinence, anal	Incontinence, anal	Occasional use of pads required	Daily use of pads required	Interfering with ADL; operative intervention indicated	Permanent bowel diversion indicated	Death
<del>Mucositis stomatitis</del> (clinical exam)	<del>Mucositis</del> (clinical exam)	<del>Erythema</del> of the mucosa	Patchy ulcerations or <del>pseudomembranes</del>	Confluent ulcerations or <del>pseudomembranes</del> ; bleeding with minor trauma	Tissue necrosis; significant spontaneous bleeding; life-threatening consequences	Death
<del>Proctitis</del>	<del>Proctitis</del>	Rectal discomfort, intervention not indicated	Symptoms not interfering with ADL; medical intervention indicated	Stool incontinence or other symptoms interfering with ADL; operative intervention indicated	Life-threatening consequences (e.g., perforation)	Death
Pain - Select:	Rectal Pain	Mild pain not interfering	Moderate pain; pain or	Severe pain; pain or	Disabling	-



# ONTOLOGIA TUMORE DEL RETTO

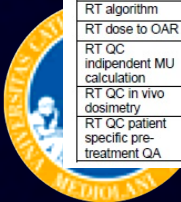
- **209 variabili analizzate:**
- **Research level: archiviazione di dati utili**

Research Level		
Table 1 Overview data collection – VATE Project		
Variables	Definition	Measurement
<b>Eligibility criteria</b>		
<b>General characteristics</b>		
Patient number	Master Patient Index (MPI)	Automatically generated number to identify patient
Study/Trial number	Protocol number	number
Medication	Concomitant medication (not therapeutic)	According to the Anatomical Therapeutic Chemical (ATC) Classification System <a href="http://www.who.int/atcddd/index/">Table 4</a> <a href="http://www.who.int/atcddd/index/">http://www.who.int/atcddd/index/</a>
Pre-existing QoL general challenges	Record the worst grade of general complaints according to the EORTC QLQ-C30 and EQ-DL5, which occurred within 4 weeks before the date of histology	Appendix C1 – Appendix C2
Pre-existing QoL rectal challenges	Record the worst grade of rectal complaints according to the EORTC QLQ-C29, which occurred within 4 weeks before the date of histology	Appendix C3
<b>Tumor characteristics</b>		
Tumor Markers		0: none 1: K-ras positive 2: EGFR positive 3: HER-Neu 4: p53 5: CEA 6: Chromogranin A 7: CDX2 8: CK20 9: MUC2 999: missing data
Tumor Markers - specimen		0: Biopsy 1: Surgical specimen
Diagnostic CT	DICOM	
Diagnostic PET	DICOM	
Diagnostic MR	DICOM	
<b>Radiotherapy treatment characteristics (T+N)</b>		
Planning CT	DICOM	
Treatment planning-CT	DICOM	
Treatment planning-RTSTRUCT	DICOM	
Treatment planning-RTPLAN	DICOM	
Treatment planning-RTDOSE	DICOM	
RT algorithm	AAA, Acuros, Pencil etc.	
RT dose to OAR	DVH	
RT QC independent MU calculation	Yes/No	
RT QC in vivo dosimetry	Mosfetm diode, EPID	
RT QC patient specific pre-treatment QA	Phantom, EPID, none	

Radiotherapy treatment characteristics (M+)		
Planning CT	DICOM	
Treatment planning-CT	DICOM	
Treatment planning-RTSTRUCT	DICOM	
Treatment planning-RTPLAN	DICOM	
Treatment planning-RTDOSE	DICOM	
RT algorithm	AAA, Acuros, Pencil etc.	
RT dose to OAR	DVH	
RT QC independent MU calculation	Yes/No	
RT QC in vivo dosimetry	Mosfetm diode, EPID	
RT QC patient specific pre-treatment QA	Phantom, EPID, none	
<b>Staging (in case of preoperative treatment)</b>		
Diagnostic CT	DICOM	
Diagnostic PET	DICOM	
Diagnostic MR	DICOM	
<b>Outcome</b>		
FUP-Acute QoL general challenges	Record the worst grade of general complaints according to the EORTC QLQ-C30 and EQ-DL5, which occurred within 3 months after the end of radiotherapy	Appendix C1 – Appendix C2
FUP-Acute QoL rectal challenges	Record the worst grade of rectal complaints according to the EORTC QLQ-C29, which occurred within 3 months after the end of radiotherapy	Appendix C3
Follow-up imaging	CT, PET, MR	0: No imaging FUP 1: CT 2: PET 3: MR 999: missing data
Diagnostic CT	DICOM	
Diagnostic PET	DICOM	
Diagnostic MR	DICOM	

Table 4: Concomitant medication

Medication code	Agents
0	None
1	Cardiac Therapy
2	Antihypertensives
3	Diuretics
4	Beta blocking agents
5	Calcium channel blockers
6	Agents acting on the renin-angiotensin system
7	Lipid modifying agents
8	Drugs for obstructing airway disease
9	Insulins and analogues
10	Blood glucose lowering drugs, exl insulins
999	Missing data





# Why Semantic Web?

## Ideas of the semantic web

- A **web of data** (now unstructured)
- **Resource Description Framework** (RDF)
  - **Subject-Predicate-Object**
  - **Patient1-hasSex-Male**





# Why Semantic Web?

- *Closed world assumption*
  - *What is not known  
to be true must be false*
- *Need to create a schema up front.*
- *Coordination necessary between centers*
- *SQL flavors*
- *Access via dedicated db connectors*





# Why Semantic Web?

## Relational databases:

- Ontology is mapped through relations between tables
- Both tables and relations are structural elements of the database
- Queries against the database are indissolubly tied to tables and relations.
- As a consequence, ontology is statically tied to the database structure
- In order to query the data contained in the repository, one needs to know explicitly the ontology mapping of the database (at the level of tables and relations and their meaning)
- Dynamically changing or simply expanding structures (toxicity, scoring systems, ...) require an IT expert for implementation into the database structure
- New members of a data collection party must project their data into the provided fields structure and need knowledge of Ontology representation. New fields or tables can only be added with the intervention of IT experts who perform structural changes





# Why Semantic Web?

- *Open world assumption*

- *What is not known*

*to be true is unknown*

- *Schema is flexible and never finished*
- *Easier to model complex relationships*
- *Standard query language SPARQL*
- *Access via http*
- *Web scalable*





# Why Semantic Web?

## Semantic Web

- Knowledge is contained in self-consistent data records
- The meaning of each record does not rely on other database structures nor content
- Ontology is encoded in a managed central repository; descriptions are not encoded in a database structure: instead, they are described in near plain language accessible to domain experts (clinicians) without IT expert implementations
- Dynamically expanding data structures require no intervention at all by IT experts
- New properties are added to the central Ontology repository.
- New members add all their data by using existing Ontology specifications or adding their own. All the knowledge they may need in order to adhere to the data collection party is exposed by the Ontology repository. There is virtually no need of further intervention by IT experts
- The system is open to future developments up to natural language queries





# Ontology

## Step 1

- *Similar to defining a database schema*
- *Define the main subjects*
  - *Patient, Disease, Treatment*
- *Define the predicates*
  - *hasSex, wasStagedWith, hasIntent*
- *Define the range of objects*
  - *NCI Thesaurus terms, CTC, ICD, etc.*





## Step 1 : Results

## Tools: Google Docs & Ontomaton





# *Proof of concept*

**1570** *Chrysomelidae: Chrysomelinae: Alticinae: Alticini*. *Altica* sp. n. (Fig. 69). Length 1.8 mm. Head black; antennae black; pronotum black; elytra black with yellowish brown spots; legs black.

# SPARQL Query

1. The first step is to identify the problem or question that needs to be answered. This involves understanding the context and the specific requirements of the task.

[Results](#) [Browse](#) [Go](#) [Index](#)

SPARGE TESTS

[illegible]

## SPARQL Result





# *Proof of concept*

Findings		Findings	
1. The system does not have a secure login mechanism.	High	12. The system does not have a secure login mechanism.	High
2. The system does not have a secure password policy.	High	13. The system does not have a secure password policy.	High
3. The system does not have a secure session management.	High	14. The system does not have a secure session management.	High
4. The system does not have a secure data storage.	High	15. The system does not have a secure data storage.	High
5. The system does not have a secure data transmission.	High	16. The system does not have a secure data transmission.	High
6. The system does not have a secure backup and recovery mechanism.	High	17. The system does not have a secure backup and recovery mechanism.	High
7. The system does not have a secure audit and logging mechanism.	High	18. The system does not have a secure audit and logging mechanism.	High
8. The system does not have a secure user management mechanism.	High	19. The system does not have a secure user management mechanism.	High
9. The system does not have a secure role-based access control mechanism.	High	20. The system does not have a secure role-based access control mechanism.	High
10. The system does not have a secure data backup and recovery mechanism.	High	21. The system does not have a secure data backup and recovery mechanism.	High
11. The system does not have a secure data backup and recovery mechanism.	High	22. The system does not have a secure data backup and recovery mechanism.	High

# Federated SPARQL Query

## SPARQL Result

***In this federated query the data is linked to the NCI Thesaurus to get a readable label***





# *Knowledge Based Oncology*

## INDIVIDUALIZED

- Tailoring treatments by prognostic/predictive features

Clinical  
decision

## ADAPTIVE

- Tailoring treatments by continuous monitoring

## MODELLING

- Prediction by multidimensional large databases





# Classic ontology

The man  
is constitutionally oriented  
to be more.....

....do more,  
know more  
and have more



Benedetto XVI, Caritas in veritate, 2010